REMARKS

Objections to the Specification

The specification stands objected to for referring to Examples 2-8 which the Office Action states are not included in the specification. The specification at page 69 does include Example 2. The specification has been amended to remove the reference to Examples 3-8. The objection should therefore be withdrawn.

The specification also stands objected to for allegedly failing to have appropriate SEQ ID NOS for Figures 8 and 9 in the "Brief Description of the Drawings." However, SEQ ID NOS corresponding to Figures 8 and 9 were added in a Preliminary Amendment dated May 16, 2002 in the "Brief Description of the Drawings." The objection should therefore be withdrawn.

Claim Rejections - 35 U.S.C. § 103

Claims 1-12, 20-39, and 45-65 stand rejected as allegedly being obvious in view of Shoyab, et al (1991, '510). The Office Action at page 3 states that Shoyab teaches epthelins, antibodies against epithelins, expression of epithelin in various tissues and the utility of epithelin as a diagnostic for tumorigenicity. Shoyab states that "[t]he presence and levels of epithelins in body fluids and tissues may be directly or inversely related to cancer or other growth related diseases." WO 91/15510 ("Shoyab"), page 30, lines 27-31. According to the Office Action this passage in Shoyab suggests Applicant's claimed invention. Applicant respectfully traverses this rejection.

Shoyab states that GP88 is an anti-proliferative protein. In contrast, the present Applicant has shown that GP88 is a tumorigenic factor and therefore elevated levels of GP88 are an indicator for cancer. The Shoyab reference teaches the opposite of the present Applicant's discovery.

According to Shoyab:

> notwithstanding their functional differences, both epithelin 1 and epithelin 2 may be useful as anti-tumor agents since they both demonstrate the ability to inhibit the growth of neoplastic cells, although applicants' initial data suggests that epithelin 1 may be a more powerful and/or effective tumor inhibitor. [Shoyab, '192 at col. 15, lines 16-21][emphasis added].

Shoyab further states that "[e]pithelins and related derivatives, analouges, and peptides thereof may be used along or with at least one other anti-proliferative compound, including, for example, an interferon, TFG-β (sic), tumor necrosis factors, etc. in the treatment of neoplastic and other growth related diseases. Carcinomas may also be treated by inducing production of epithelins in the carcinoma cells." Shoyab, '510 at page 28, lines 16-21 (emphasis added). According to Shoyab, epithelins are anti-proliferative compounds useful in the treatment of tumors. Thus, Shoyab teaches away from Applicant's invention.

According to the Office Action, "Shoyab, et al. further teach an in vivo role for epithelin in terminal differentiation of cell." Office Action at page 3. Terminal differentiation and arrested tumor growth are the precise opposite of Applicant's discovering that GP88 is a highly tumorigenic protein. According to Shoyab, "the ability of epithelin to reactivate normal cellular differentiation in tumors and, ultimately, to arrest continued tumor growth may find valuable use in tumor therapy regimens." Shoyab at page 28, lines 12-15 (emphasis added). Therefore, Shoyab teaches that epithelins are a marker for terminal differentiation, and not for tumorigenic cell growth. In contrast, the Applicant's claims recite that the ratio of GP88 positive cells to the total number of cells in a biological sample is indicative of tumorigenicity. Shoyab amply demonstrates the patentability, not the obviousness, of Applicant's claimed invention. Following the teachings of Shoyab would lead to an incorrect and possibly dangerous diagnosis by indicating that a patient is recovering rather than suffering from tumorigenic cell growth.

The Office Action at page 3 alleges that "it would be obvious to use the method to determine antineoplastic effects of antiestrogen therapy in an estrogen receptor positive patient since epithelin is expressed in breast cancer (p.11)." This statement in the Office action is a leap of logic, and based on a hindsight reading of Applicant's own disclosure. Shoyab does not include one word about antiestrogens, antiestrogen therapy and does not remotely suggest any connection between antiestrogens and the level of GP88. Shoyab merely states that epithelin is expressed in breast tissue, but does not say anything about expressing breast cancer. Expression of a particular protein in breast tissue is unrelated to whether the protein is present in breast cancer. In addition, as demonstrated above, Shoyab teaches away from Applicant's claimed invention by teaching that epithelin is an anti-proliferative rather than tumorigenic.

agree

Shoyab's sole passage relied on in the Office Action that epithelins "may" be related to "growth related diseases" simply provides no disclosure from which one of skill in the art would have any reasonable expectation of success in diagnosing tumorigenicity by measuring GP88 levels. The Shoyab references actually teach away from Applicant's invention by teaching that the epithelins inhibit the growth of neoplastic cells, i.e., that increased levels of epithelins are associated with non-tumorigenic, rather than tumorigenic cells. Shoyab cannot possibly render the present claims obvious since Shoyab teaches away from the invention. Accordingly, the rejection of claims 1-12, 20-39, and 45-65 under 35 U.S.C. § 103 should be withdrawn.

Attached hereto is a marked-up version of the changes made to the specification by the current amendment. The attached page is captioned **"Version with markings to show changes made."**

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejection of the claims and to pass this application to issue.

Dated: October 29, 2002

Respectfully submitted,

By _____

James W. Brady, Jr.
Registration No.: 32,115
Jeremy A. Cubert
Registration No.: 40,399
DICKSTEIN SHAPIRO MORIN &
OSHINSKY LLP
2101 L Street NW
Washington, DC 20037-1526
(202) 785-9700
Attorneys for Applicant

Version With Markings to Show Changes Made

[0072] For Northern blot analysis of GP88 mRNA expression in human cell lines, a 672 bp human GP88 cDNA probe was developed corresponding to nucleotide 1002 to 1674 (corresponding to amino-acid sequence 334-558) of human GP88. [See example 8 for a detailed and specific description of the Northern blot analysis method used in the preferred embodiments.]